IN THE CLAIMS

Amend the claims as indicated below by the markings. Cancel claims 1, 21 and 29 without prejudice.

Claims 1 - 4. (Cancelled)

5. (Currently Amended) The transgenic mutant mouse according to claim 33 [[1]], wherein the genome of the transgenic mutant mouse comprises a transgene within the disrupted region introduced in the endogenous Sigma-1 receptor gene that comprises a sequence encoding a positive selection marker.

Claims 6 - 8. (Cancelled)

9. (Currently Amended) A homologous recombination vector with a positive-negative selection marker identified as pHR53TK, deposited in Spanish Type Culture Collection (CECT) of the University of Valencia with access number CECT 5737 suitable for producing a non-human mutant mammal having a disruption in a gene of an endogenous Sigma-1 receptor and having a phenotype characterized by a statistical difference in hypermotility response compared to wild mice.

Claims 10 – 16. (Cancelled)

17. (Currently Amended) An isolated cell from a transgenic mouse, deficient in an endogenous Sigma-1 receptor, according to claim 33 [[1]], or its offspring.

18. (Previously presented) The cell according to claim 17, comprising one or both mutated alleles of the Sigma-1 receptor gene.

19. (Previously presented) The cell according to claim 17, wherein the cell is propagated.

20. (Previously Presented) The offspring of a transgenic mutant mouse deficient in an endogenous Sigma-1 receptor, according to claim 33 [[1]].

Claims 21 – 27. (Cancelled)

28. (Currently Amended) The cell according to claim 40 [[19]] wherein the cell is immortalized.

Claims 29 - 32. (Cancelled)

33.(New) A transgenic mutant mouse, comprising a mouse whose genome includes a mutation having a disruption in a gene of an endogenous Sigma-1 receptor, said gene disruption giving rise to a fertile homozygous transgenic mutant mouse lacking detectable levels of endogenous Sigma-1 receptor, said transgenic mutant mouse having a phenotype characterized by a statistical difference in hyperactivity response compared to wild mice.

34. (New) A transgenic mutant mouse as claimed in claim 33, wherein said mutant mouse is obtainable by the use of the vector identified as pHR53TK that is deposited in the CECT under access number CECT 5737, to insert a functional disruption in the endogenous Sigma-1 receptor.

35.(New) A transgenic mutant mouse as claimed in claim 33, wherein said mutant mouse is homozygous for the mutation.

36.(New) A transgenic mutant mouse as claimed in claim 33, wherein said mutant mouse is heterozygous for the mutation.

37.(New) A transgenic mutant mouse wherein said transgenic mutant mouse is an offspring of a transgenic mutant mouse according to claim 33.

38.(New) A transgenic mutant mouse as claimed in claim 33, wherein the genome of the transgenic mutant mouse comprises a transgene within the mutation introduced in the endogenous Sigma-1 receptor gene that comprises a gene encoding a positive or negative selection marker.

39.(New) A transgenic mutant mouse as claimed in claim 38, wherein said transgene comprises the neomycin phototransferase (neo) gene.

40.(New) An isolated cell of a transgenic mutant mouse wherein said isolated cell is a cell of a transgenic mutant mouse according to claim 33.

41. (New) An isolated cell of a transgenic mutant mouse as claimed in claim 40, wherein said cell is heterozygous for the mutated endogenous Sigma receptor allele.

42.(New) An isolated cell of a transgenic mutant mouse as claimed in claim 40, wherein said cell is homozygous for the mutated endogenous Sigma receptor allele.

43. (New) A process for making a mutant mouse, comprising the steps of:

introducing a functional disruption in an endogenous Sigma-1 receptor gene present in a cell genome by homologous recombination in said cell between an allele of an endogenous Sigma-1 receptor gene and a homologous recombination vector with positive-negative selection,

selecting the recombinant homologues by the positive-negative selection technique,

introducing said recombinant homologues in embryos,

implanting said embryos in receptor pseudogestating female mammals,

carrying, by the female mammals, the embryos to term,

selecting chimeras able to efficiently transmit the genotype of the recombinant homologues to their offspring by the germ line, said chimeras having a phenotype being characterized by a statistical difference in hypermotility response compared to wild mice, and

crossing said chimeras with wild-type mice to obtain heterozygous mutants to disrupt the endogenous Sigma-1 receptor.

44. (New) A process as claimed in claim 43, further comprising the step of: crossing said heterozygous mutants with one another to obtain a mutant homozygous mouse.

45.(New) A process as claimed in claim 43, wherein said step of introducing the functional disruption in the endogenous Sigma-1 receptor gene is performed using a vector identified as pHR53TK that is deposited in the CECT under access number CECT 5737.

46.(New) A homologous recombination vector with positive-negative selection useful for introducing a functional disruption in a Sigma receptor gene, comprising:

a first homology region, positioned at the 5' end of a nucleotide sequence encoding a positive selection marker, wherein said first homology region has a nucleotide sequence that is substantially identical to a first sequence of a Sigma-1 receptor gene;

a nucleotide sequence encoding a positive selection;

a second homology region, positioned at the 3' end of said nucleotide sequence encoding a positive selection marker, wherein said second homology region has a nucleotide sequence that is substantially identical to a second sequence of the Sigma-1 receptor gene, the second Sigma-1 receptor gene being positioned 3' to the aforementioned first sequence of the Sigma-1 receptor gene in a wild type endogenous Sigma-1 gene; and

a nucleotide sequence encoding a negative selection marker,

wherein a mutant non-human mammal being homologous to said functional disruption in said Sigma-1 receptor gene is of a phenotype characterized by a difference in hyperactivity response induced by the SKF-10047 ligand compared to wild mice.

47.(New) A homologous recombination vector as claimed in claim 46, wherein said mutant non-human mammal is a mutant mouse that lacks any detectable level of Sigma-1 receptor.

48.(New) A homologous recombination vector as claimed in claim 46 wherein said vector is identified as pHR53TK that is deposited in the CECT under access number CECT 5737.